



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

SEP 23 1996

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

**MEMORANDUM**

SUBJECT: PP# 6F04748. Difenconazole (Dividend) in or on Barley, Oats, and Triticale. **Evaluation of Residue Data and Analytical Methods.** MRID# 440560-01. Case 287954. Chemical 128847. Barcode D228403. CBTS# 17407.

FROM: G.F. Kramer, Ph.D., Chemist *[Signature]*  
Tolerance Petition Team I  
Chemistry Branch I, Tolerance Support  
Health Effects Division (7509C)

THRU: E.T. Haeberer, Acting Branch Chief *Elizabeth T. Haeberer*  
Chemistry Branch I, Tolerance Support  
Health Effects Division (7509C)

TO: C. Eiden/D. McCall  
Registration Section, RCAB  
Health Effects Division (7509C)

CIBA-GEIGY Corporation has proposed tolerances for residues of the fungicide difenoconazole  $[(2S,4R)/(2R,4S)]/[(2R,4R)/(2S,4S)]1-[2-[4-(4-chlorophenoxy)-2-chlorophenyl]-4-methyl-1,3-dioxolan-2-yl-methyl]-1H-1,2,4-triazole$  in/on barley, oats, and triticale.

The proposed tolerances, expressed as parent compound only, are:

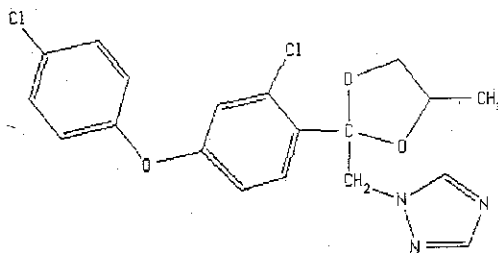
Barley, forage	--	0.05 ppm	Barley, hay	--	0.05 ppm
Barley, straw	--	0.05 ppm	Oats, forage	--	0.05 ppm
Oats, grain	--	0.01 ppm	Oats, hay	--	0.05 ppm
Oats, straw	--	0.05 ppm	Triticale, forage	--	0.05 ppm
Triticale, grain	--	0.01 ppm	Triticale, hay	--	0.05 ppm
Triticale, straw	--	0.05 ppm			

Tolerances with an expiration date of 12/31/98 are established for residues of difenoconazole *per se* in/on wheat and animal RACs under 40 CFR § 180.475(a). Tolerances for residues of difenoconazole in/on imported barley, rye and wheat grain and animal RACs are established under 40 CFR § 180.475(c) and range from 0.01-0.1 ppm.



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The structure of difenoconazole is shown below:



**Difenoconazole**

#### Executive Summary of Chemistry Deficiencies

- Interference study or selective confirmatory technique for analytical method for plants.
- Revise label by increasing triticale forage PHI or provide residue data supporting lower PHI.
- Additional storage stability data.
- Residue data for oats.
- Revised Section F.

#### CONCLUSIONS

1. All product chemistry data requirements for difenoconazole TGAI are fulfilled (PP#2F4107; Memo, G. Kramer 1/18/95).
2. The petitioner has proposed an adequate set of directions for use of Dividend on barley, oats, and triticale.
3. The petitioner has previously submitted the results of two confined crop rotation studies using radiolabelled difenoconazole (PP#2F4107; Memo, G. Kramer 9/13/95). In the RACs of all rotational crops planted 30-33 days after application of

difenoconazole, the TRR was  $<0.01$  ppm. These results support the proposed 30 day plantback restrictions for all rotational crops.

4. The nature of the residue is understood in tomatoes, potatoes and wheat. The HED Metabolism Committee has determined that none of the difenoconazole metabolites warrant inclusion in the tolerance regulation or separate regulation or inclusion in the dietary risk assessment or additional metabolism or toxicological studies (Memo, G. Kramer 7/22/94).

5. CBTS previously concluded that nature of the residue in animals is understood for the purposes of the use on wheat (PP#2F4107; Memo, G. Kramer 6/16/94). CBTS is willing to extend this conclusion to the proposed uses on oats, barley and triticale. The HED Metabolism Committee has determined that none of the difenoconazole metabolites warrant inclusion in the tolerance expression for animal RACs or separate regulation or inclusion in the dietary risk assessment or additional metabolism or toxicological studies (Memo, G. Kramer 7/22/94).

6a. Barley samples were analyzed by the enforcement method, AG-575B. This GC/NPD method was reviewed previously by CBTS (PP#2E4051; Memo, R. Lascola 12/22/92). Acceptable recoveries were obtained for barley RACs (overall average recovery of  $105 \pm 12.9\%$ ).

6b. As no confirmatory method is available, the specificity of the analytical enforcement method should be demonstrated by performing an interference study with all pesticides for which tolerances are established on barley and oats. Alternatively, the petitioner may propose a selective (i.e., GC/MS) confirmatory technique.

6c. CBTS concludes that Method AG-575B is adequate for data gathering purposes. A conclusion on the adequacy of the method for enforcement of the proposed tolerances will be withheld pending demonstration of method specificity (interference study or selective confirmatory technique).

7. The RAC samples from the field residue studies were stored for a maximum of 23 months. Difenoconazole has been previously shown to be stable in potatoes and tomatoes for up to 2 years of storage and in wheat forage and bananas for 1 year (Memos, R. Lascola 10/26/92 and G. Kramer 3/30/94 & 2/23/96). Further studies are needed to demonstrate storage stability in the RACs wheat (or barley) grain and straw (PP#2F4107; Memo, G. Kramer 6/16/94). The petitioner reports that a 2-year storage stability study on wheat RACs is in progress.

8a. A total of nine barley residue trials were conducted in 1994/95 in eight different states. These trials were located in Regions 2 (1 trial), 5 (2 trials), 7 (2 trials), 9 (2 trials), 10 (1 trial) and 11 (3 trial). Barley was planted following treatment with difenoconazole at a rate of 10.9 grams ai/100 lbs. seed (1X).

The difenoconazole residues were <LOQ (0.01 ppm in grain; 0.05 ppm in forage, straw, and hay) in all samples.

8b. The number and location of these trials closely matches that required by CBTS. These results thus support the proposed barley tolerances.

9a. No residue data were submitted for triticale. However, 40 CFR § 180.1(h) specifies that wheat tolerances also include triticale. As wheat tolerances for difenoconazole are also established, triticale may be added to the Dividend labels without submission of additional data. However, the petitioner has proposed a shorter PHI for triticale forage (30 days) than is currently established for wheat forage (55 days). Residue data for triticale forage should be provided to support the proposed 30-day PHI or the Dividend labels modified to specify a 55-day PHI for triticale forage.

9b. CBTS notes that the conditions applied to the wheat registration will also apply to the triticale registration. Section F should be modified by removal of the proposed triticale tolerances.

10. No residue data were submitted for oats. The petitioner claims that the wheat and barley data may be translated to oats. Based on the presence of detectable residues in some of the wheat and barley field trials reflecting seed treatment applications at roughly the rate proposed in this petition, CBTS is not willing to waive the need for oat field trials. However, CBTS will take into account the data on wheat and barley when determining the number of trials needed for oats. Provided residues in oat RAC's are less than the LOQ at all sites, the number of trials for oats may be reduced from the usually required 12 (for a use with <LOQ residues) to 6.

11. Adequate processing data are available for wheat (Memos, R. Lascola 10/26/92 and G. Kramer 3/30/94). Concentration of difenoconazole residues was not observed in any wheat fraction. CBTS is willing to translate these results to barley and oats and conclude that food/feed additive tolerances are not required for this petition provided quantifiable residues are not found in oat grain.

12. As the tolerances associated with the present petition are less than or equal to those established on wheat and the grains in this petition would be substituted for wheat in animal diets, there is no potential for increased livestock dietary burdens as a result of these proposed tolerances on oats, barley and triticale. The currently established permanent tolerances for residues of difenoconazole on meat, milk and eggs are thus adequate to support the proposed new uses on barley, triticale and oats.

13. There is neither a Codex proposal, nor Canadian or Mexican limits for residues of difenoconazole in barley, oats, and triticale. Therefore, a compatibility issue is not relevant to the proposed tolerance. A copy of the IRLS sheet is attached to this memorandum.

14. HED notes that the Food Quality Protection Act of 1996 has amended and strengthened the standard for establishing tolerances under the FFDCA. OPP is still assessing the full impact of this change in the law on the tolerance-setting process and plans to issue guidelines concerning the establishment of tolerances under the amended statute. All tolerance petitions have to meet the requirements of the FFDCA as amended by the FQPA and OPP may require additional data to determine if the terms of the amended statute are met.

#### RECOMMENDATIONS

CBTS recommends against the proposed tolerance for difenoconazole in/on barley, oats, and triticale for reasons detailed in conclusions 6b, 6c, 7, 9a, 9b, 10 and 14 .

#### DETAILED CONSIDERATIONS

##### Product Chemistry

All product chemistry data requirements for difenoconazole TGAI are fulfilled (PP#2F4107; Memo, G. Kramer 1/18/95).

##### Formulation

Difenoconazole is formulated as the following flowable concentrates: Dividend 0.15 FS (EPA Reg. No. 100-777) containing 1.54% ai, Dividend Twin-Pak (EPA Reg. No. 100-740) containing 32.8% ai, and Dividend 0.31 FS (EPA Reg. No. 100-778) containing 3.15% ai.

##### Proposed Use

Dividend 0.15 FS and Dividend 0.31 FS are applied directly to seed and Dividend Twin-Pak is applied as a water-based slurry by mixing

with up to 16 oz. water per 100 lbs. seed. The maximum use rate is 10.9 grams or 0.38 oz. ai/100 lbs. seed.

The label contains the following restrictions: a) do not use treated seed for feed, food or oil; b) barley, oat, and triticale green forage may not be grazed until 30 days after planting; and c) do not plant rotational crops within 30 days of planting treated seeds.

The petitioner has proposed an adequate set of directions for use of Dividend on barley, oats, and triticale.

#### Rotational Crop Studies

The petitioner has previously submitted the results of two confined crop rotation studies using radiolabelled difenoconazole (PP#2F4107; Memo, G. Kramer 9/13/95). In the RACs of all rotational crops planted 30-33 days after application of difenoconazole, the TRR was <0.01 ppm. These results support the proposed 30 day plantback restrictions for all rotational crops.

#### Nature of Residue- Plants

The nature of the residue is understood in tomatoes, potatoes and wheat. The major terminal residues in wheat grain are the metabolites triazole and triazole acetic acid; and in wheat straw and forage, are triazole alanine, triazole acetic acid and CGA-205375. The parent was not detected in grain and comprised 7-8% of the TRR in forage and 0.3-0.4% of the TRR in straw (PP#2F4107; Memo, G. Kramer 6/16/94).

The HED Metabolism Committee has determined that none of the difenoconazole metabolites warrant inclusion in the tolerance expression for plant RACs or separate regulation or inclusion in the dietary risk assessment or additional metabolism or toxicological studies (Memo, G. Kramer 7/22/94).

#### Nature of Residue- Animals

CBTS previously concluded that nature of the residue in animals is understood for the purposes of the use on wheat (PP#2F4107; Memo, G. Kramer 6/16/94). For any future petition in which there is a greater potential for transfer of residues to meat, milk, and eggs;

additional animal metabolism studies were required. However, as the tolerances associated with the present petition are less than or equal to those established on wheat and the grains in this petition would be substituted for wheat in animal diets, there is no potential for increased livestock dietary burdens as a result of these proposed tolerances on oats, barley and triticale. CBTS is thus willing to extend the conclusion for the use on wheat to cover the proposed uses on oats, barley and triticale.

The HED Metabolism Committee has determined that none of the difenoconazole metabolites warrant inclusion in the tolerance expression for animal RACs or separate regulation or inclusion in the dietary risk assessment or additional metabolism or toxicological studies (Memo, G. Kramer 7/22/94).

#### **Analytical Methodology- Plants**

Barley samples were analyzed by the enforcement method, AG-575B (MRID# 428065-04). This GC method was reviewed previously by CBTS (Memo, R. Lascola 12/22/92). Acceptable recoveries were obtained for barley RACs (overall average recovery of  $105\% \pm 12.9$ ,  $n=37$ ).

**Specificity:** As no confirmatory method is available, the specificity of the analytical enforcement method should be demonstrated by performing an interference study with all pesticides for which tolerances are established on barley and oats. Alternatively, the petitioner may propose a selective (i.e., GC/MS) confirmatory technique.

**Conclusions:** CBTS concludes that Method AG-575B is adequate for data gathering purposes. A conclusion on the adequacy of the method for enforcement of the proposed tolerances will be withheld pending demonstration of method specificity (interference study or selective confirmatory technique).

#### **Storage Stability Studies**

The RAC samples from the field residue studies were stored for a maximum of 23 months. Difenoconazole has been previously shown to be stable in potatoes and tomatoes for up to 2 years of storage and in wheat forage and bananas for 1 year (Memos, R. Lascola 10/26/92 and G. Kramer 3/30/94 & 2/23/96). Further studies are needed to demonstrate storage stability in the RACs wheat (or barley) grain and straw (PP#2F4107; Memo, G. Kramer 6/16/94). The petitioner reports that a 2-year storage stability study on wheat RACs is in progress.

**Magnitude of Residue- Barley**

Submitted with this petition:

Difenoconazole - Magnitude of the Residue in or on Spring Barley Following Seed Treatment Application of Dividend.  
MRID# 440560-01

A total of nine field residue trials were conducted in 1994/95 in eight different states. These trials were located in Regions 2 (1 trial), 5 (2 trials), 7 (2 trials), 9 (2 trials), 10 (1 trial) and 11 (3 trial). Barley was planted following treatment with difenoconazole at a rate of 10.9 grams ai/100 lbs. seed (1X). A single trial also included a 2X treatment. Two replicate forage samples were harvested 32-152 days after planting; hay, 54-191 days; and grain and straw, 89-224 days. The samples were frozen and shipped to Ciba (NC) for analysis. Sample analysis for difenoconazole was performed using the proposed enforcement method. The method was validated over a range of 0.01-5.0 ppm. The average recovery was  $111 \pm 11.2\%$  (n=9) in grain,  $94 \pm 14.9\%$  (n=10) in forage,  $111 \pm 7.8\%$  (n=9) in hay, and  $106 \pm 8.8\%$  (n=9) in straw. Analyses of the treated samples showed that the difenoconazole residues were <LOQ (0.01 ppm in grain; 0.05 ppm in forage, straw, and hay) in all samples (Table 1).

**Conclusions:** The number and location of these trials closely matches that required by CBTS: nine trials located in Regions 1 or 2 (1 trial), 5 (2 trials), 7 (3 trials), 9 (1 trial), 10 (1 trial) and 11 (3 trial) (*EPA Guidance on Number and Location of Domestic Crop Field Trials for Establishment of Pesticide Residue Tolerances*, 6/2/94). These results thus support the proposed barley tolerances.



Table 1- Difenoconazole residues in barley after seed treatment.

State	Treatment Rate	RAC	PHI (Days)	Residues (ppm)
ID	1X	Forage	46	<0.05, <0.05
		Hay	82	<0.05, <0.05
		Straw	109	<0.05, <0.05
		Grain	109	<0.01, <0.01
ND	1X	Forage	34	<0.05, <0.05
		Hay	67	<0.05, <0.05
		Straw	89	<0.05, <0.05
		Grain	89	<0.01, <0.01
	2X	Forage	34	<0.05
		Hay	67	<0.05
		Straw	89	<0.05
		Grain	89	<0.01
MN	1X	Forage	43	<0.05, <0.05
		Hay	54	<0.05, <0.05
		Straw	95	<0.05, <0.05
		Grain	95	<0.01, <0.01
MT	1X	Forage	38	<0.05, <0.05
		Hay	65	<0.05, <0.05
		Straw	107	<0.05, <0.05
		Grain	107	<0.01, <0.01
ND	1X	Forage	32	<0.05, <0.05
		Hay	66	<0.05, <0.05
		Straw	91	<0.05, <0.05
		Grain	92	<0.01, <0.01
SD	1X	Forage	34	<0.05, <0.05
		Hay	65	<0.05, <0.05
		Straw	94	<0.05, <0.05
		Grain	94	<0.01, <0.01
VA	1X	Forage	152	<0.05, <0.05
		Hay	191	<0.05, <0.05
		Straw	224	<0.05, <0.05
		Grain	224	<0.01, <0.01

State	Treatment Rate	RAC	PHI (Days)	Residues (ppm)
CO	1X	Forage	76	<0.05, <0.05
		Hay	100	<0.05, <0.05
		Straw	123	<0.05, <0.05
		Grain	123	<0.01, <0.01
CA	1X	Forage	68	<0.05, <0.05
		Hay	130	<0.05, <0.05
		Straw	195	<0.05, <0.05
		Grain	195	<0.01, <0.01

#### Magnitude of Residue- Triticale

No residue data were submitted for triticale. However, 40 CFR § 180.1(h) specifies that wheat tolerances also include triticale. As wheat tolerances for difenoconazole are also established, triticale may be added the Dividend labels without submission of additional data. However, the petitioner has proposed a shorter PHI for triticale forage (30 days) than is currently established for wheat forage (55 days). Residue data for triticale forage should be provided to support the proposed 30-day PHI or the Dividend labels modified to specify a 55-day PHI for triticale forage.

CBTS notes that the conditions applied to the wheat registration will also apply to the triticale registration. Section F should be modified by removal of the proposed triticale tolerances.

#### Magnitude of Residue- Oats

No residue data were submitted for oats. The petitioner claims that the wheat and barley data may be translated to oats. CBTS has considered all the residue data for wheat and barley reflecting seed treatment and concludes that some field trials are still required for oats. If detectable residues had not been found in any of the wheat and barley trials, especially from exaggerated rate studies, CBTS would be willing to waive the requirement for data on oats. However, as discussed in our reviews of PP#2F4107 (G. Kramer, 3/30/94) and PP#2E4051 (R. Lascola, 10/26/92), detectable residues were found in some grain, forage and straw samples following applications at roughly the rate proposed in this

petition. Therefore, field trials on oats are required. However, CBTS will take into account the data on wheat and barley when determining the number of trials needed for oats. Provided residues in oat RAC's are less than the LOQ at all sites, the number of trials for oats may be reduced from the usually required 12 (for a use with <LOQ residues) to 6.

#### Magnitude of the Residue- Processed Fractions

Adequate processing data are available for wheat (Memos, R. Lascola 10/26/92 and G. Kramer 3/30/94). Concentration of difenoconazole residues was not observed in any wheat fraction. CBTS is willing to translate these results to barley and oats and conclude that food/feed additive tolerances are not required for this petition provided quantifiable residues are not found in oat grain.

#### Magnitude of the Residue- Ruminants

As the tolerances associated with the present petition are less than or equal to those established on wheat and the grains in this petition would be substituted for wheat in animal diets, there is no potential for increased livestock dietary burdens as a result of these proposed tolerances on oats, barley and triticale. The currently established permanent tolerances for residues of difenoconazole on meat, milk and eggs are thus adequate to support the proposed new uses on barley, triticale and oats.

Attachment 1- IRLS Sheet

cc: PP#6F04748, Kramer, R.F., Circ., J. Stone/C. Giles-Parker (RD, 7505C)  
RDI: TPT1 (9/5/96), E. Haeberer (9/23/96), R.A. Loranger (9/20/96)  
G.F. Kramer:804V:CM#2:(703)305-5079:7509C

*J. Hoes*  
*8/27/96*

Attachment:

Page 1 of 2INTERNATIONAL RESIDUE LIMIT STATUSCHEMICAL difenoconazole\*

CODEX NO. \_\_\_\_\_

CODEX STATUS:

☒ No Codex Proposal  
 Step 6 or Above

Residue (if Step 8): \_\_\_\_\_

PROPOSED U.S. TOLERANCES:Petition No. 6F04748CBTS Reviewer G.F. KramerResidue: parent only

<u>Crop(s)</u>	<u>Limit</u> <u>(mg/KG)</u>
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<u>Crop(s)</u>	<u>Limit</u> <u>(mg/KG)</u>
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Barley, forage	0.05
Barley, hay	0.05
Barley, straw	0.05
Oats, forage	0.05
Oats, grain	0.01
Oats, hay	0.05
Oats, straw	0.05
Triticale, forage	0.05
Triticale, grain	0.01
Triticale, hay	0.05
Triticale, straw	0.05

CANADIAN LIMITS:

☒ No Canadian Limits

Residue: \_\_\_\_\_

MEXICAN LIMITS:

☐ No Mexican Limits

Residue: \_\_\_\_\_

<u>Crop(s)</u>	<u>Limit</u> <u>(mg/KG)</u>
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<u>Crop(s)</u>	<u>Limit</u> <u>(mg/KG)</u>
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*barley*  
*oats*  
*wheat*

*appear to be*  
*exempted*

## NOTES

\*1-{2-[4-(4-chlorophenoxy)-2-chlorophenyl]-4-methyl-1,3-dioxolan-2-yl-methyl}-1H-1,2,4-triazole



13544

032652

Chemical:

*DIFENCONAZOLE*  
~~4,2-Dihydro-3,6-pyridazinedione~~

PC Code:

051501 *129847*

HED File Code

~~13000-Tox-Reviews~~

*11000 Chem. Review*

Memo Date:

~~07/21/70~~ *09-23-96*

File ID:

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Accession Number:

412-03-0020

HED Records Reference Center

01/23/2003